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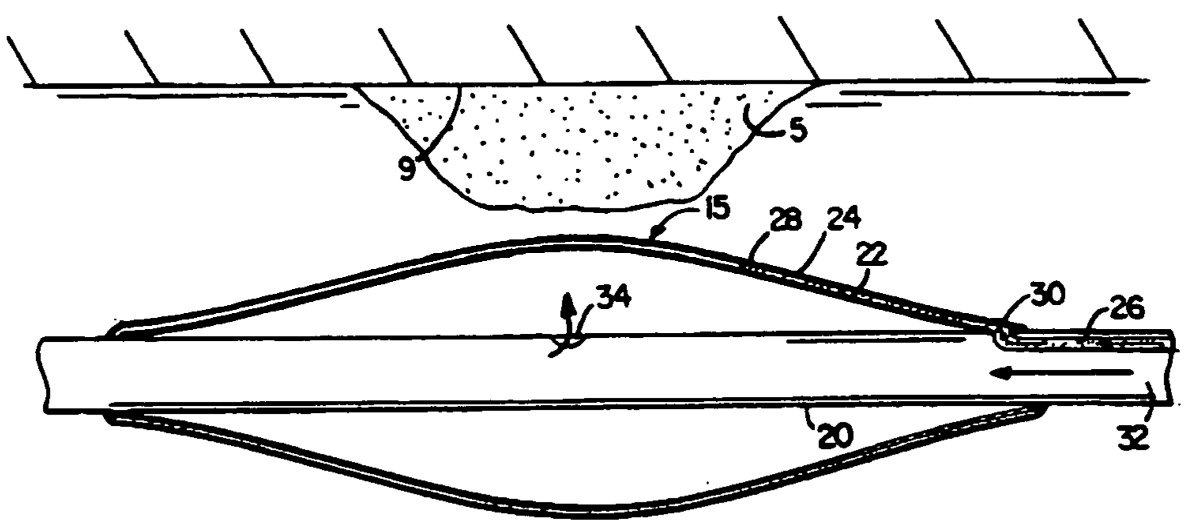

(57) Abstract

In one aspect, the invention features a catherer (20) for delivering drug to tissue at a desired location of the wall of a body lumen. The catherer (20) is constructed for insertion in a body lumen, and has a catherer shaft (32) and an expandable balloon portion mounted on the catheter shaft (32). The expandable balloon portion (15) being expandable to a controlled pressure to fill the cross section of the body lumen (9) and press against the wall of the body lumen (9). At least a portion of the exterior surface

BALLOON DRUG DELIVERY SYSTEM

Field of the Invention

The invention relates to delivery of drugs to the walls of body lumens.

Background of the Invention

Systemic administration of drugs treats the organism as a whole, even though the disease may be localized, such as occlusion of a duct or vessel. Localization of a drug poses special problems in cases involving the walls of ducts and vessels, since, by nature, these organs serve as transport systems.

Arthrosclerotic disease, for example, causes localized occlusion of the blood vessels resulting from the build-up of plaque. As the deposits increase in size, they reduce the diameter of the arteries and impede blood circulation. Angioplasty, which involves the insertion of catheters, such as balloon catheters, through the occluded region of the blood vessel in order to expand it, has been used to treat arthrosclerosis.

The aftermath of angioplasty in many cases is problematic, due to restenosis, or closing of the vessel, that can occur from causes including mechanical abrasion and the proliferation of smooth muscle cells stimulated by the angioplasty treatment. Restenosis may also occur as a result of clot formation following angioplasty, due to injury to the vessel wall which triggers the natural clot-forming reactions of the blood.

Summary of the Invention

The invention features a catheter and method for delivering drug to tissue at a desired location of the wall of a body lumen. The catheter is constructed for insertion in a body lumen and has a catheter shaft and an expandable balloon portion mounted on the catheter shaft. The expandable balloon portion is expandable to a

controlled pressure to fill the cross section of the body lumen and press against the wall of the body lumen. At least a portion of the exterior surface of the expandable balloon portion is defined by a porous membrane positioned over the surface of the balloon and creating therebetween a drug space. The porous membrane is formed of a select material and is constructed to release drug in the drug space through openings in the membrane to the outer surface of the membrane in a noninjurious low pressure manner. The drug application occurs in response to pressure applied by inflation of the balloon to compress the drug space.

Various embodiments may include one or more of the following features. The porous membrane has a series of tortuous pathways through its thickness between openings exposed to the drug space and openings exposed to the body lumen. The openings are of selected small size to prevent the flow of fluid prior to the application of pressure to the drug. The drug is an aqueous drug solution and the porous material is a hydrophobic material. The openings are in the range of about 2 to 20 μm. The membrane material is selected from the group consisting of porous fluorocarbon plastic material and ultrahigh molecular weight microporous polyethylene. The membrane comprises a plurality of layers of material, the orifice of which collectively define the tortuous pathways. The drug is an anti-thrombogenic drug selected from the group consisting of heparin, enoxaprin, aspirin, Pebac and hirudin. The drug is an antiproliferative selected from the group consisting of monoclonal antibodies, capable of blocking smooth muscle cell proliferation, heparin and enoxaprin. The method includes preparing the balloon portion by introducing an aqueous solution of the drug to the drug space, introducing the catheter to the body lumen to position

the expandable portion at the point of desired drug application, and expanding the expandable balloon portion to enable delivery of the drug by compression of the drug space. The method further comprises, deflating the balloon and repeating the preparing and expanding steps. The membrane comprises more than one layer of the material.

In general, an advantage of the invention is the application of drugs directly to the tissue within the body requiring treatment. The drug is preferably applied in a rapid but low-stress, low energy manner that does not further injure the tissue to be treated, and administration is selectively and evenly distributed over the treated area such that the drug can be taken up by tissue, without e.g. being washed away by body fluids.

Description of Preferred Embodiments

We first briefly describe the drawings.

Drawings

Fig. 1 is an enlarged, cross-sectional view of a drug delivery balloon catheter including a semi-permeable outer balloon and an inner balloon.

Figs. 1a and 1b are further enlarged schematic illustrations of a portion of Fig. 1 and show the manner in which a semi-permeable balloon prevents passage (Fig. 1a) and enables passage (Fig. 1b) of a drug, while Fig. 1c is a much enlarged cross sectional view of the region C in Fig. 1a of the membrane, illustrating tortuous pathways through the thickness of the membrane.

Description

Referring to Fig. 1, a catheter 20 carries an inner balloon 22 and an outer balloon 24, the latter including at least a portion formed of porous material 15 through which the drug may pass under conditions of pressure. The drug is introduced through a first lumen

26 into the intermediate region 28 between the balloons 22 and 24 via the first aperture 30. At the time of dilatation, inflation fluid passes through a second lumen 32 and through port 34 to inflate the inner balloon 22. Inflation of the inner balloon 22 provides the pressure needed on the drug in the intermediate region 28 to effect passage of the drug through openings of the membrane 15. The inner balloon 22 may be deflated and the intermediate region 28 refilled in order to repeat the process and to deliver the drug to various locations along the duct or vessel to repeat administration at the same location or to administer a different concentration or a different drug. In particular, a contrast material is preferably employed in the inflation fluid, which, being separated from the drug, prevents the need to pass contrast into the body lumen.

The inner balloon may be of the type used in dilatation of blood vessesl and made, for example, of a somewhat compliant material such as polyethylene that conforms to the shape of the body lumen wall or a nondistendable material such as PET. At least a portion of the outer balloon membrane may include a membrane selected such that the membrane creates sufficient resistance so that the drug weeps out of the membrane without substantial velocity or force against the vessel wall and thus the drug contacts the diseased tissue in contact with the outer surface of the membrane under substantially no pressure. This gentle application is advantageous since injury or disruption of the vessel wall is avoided. Preferably, the membrane has at least one layer of hydrophobic material having small openings, e.g. 2-20 microns, create a large pressure drop across the membrane to dissipate the pressure applied to the drug in the region 28 during balloon inflation and effect a low-energy weeping application of drug. Prior to

pressuring the drug, the small openings prevent the flow of the drug from the region 28 (or the contamination of the region 28 with body fluid from the body lumen) as further discussed below. Referring to Fig. 1c, most preferably the membrane material 24 includes a series of tortuous paths 34 through its thickness connecting openings 36 on its inner surface exposed to the region 28 and openings 38 exposed to the body lumen. The flow of drug through the pathways reduces the velocity of the drug and enables gentle application to tissue. Suitable materials include, but are not limited to, GORETEX® (a woven porous fluorocarbon plastic material) and ultrahigh molecular weight microporous polyethylene (a polyethylene material available through Millipore, Inc. and commonly used for filter membranes). Either the entire balloon 24 is formed from the semi-permeable material or a patch of the material is attached to a normal balloon e.g. by heat sealing. Other semi-permeable membranes may be formed by providing relatively large, substantially straight pathways through a polymer material and applying thereover, on the outside of the membrane, a hydrogel polymer, e.g., of polyacrylic acid of the type described in U.S. Serial No. 297,331, filed January 17, 1989, the entire contents of which are incorporated herein by reference (see also corresponding EP publication no. 0 379156 published July 25, 1990). Low energy application may also be achieved by a porous material formed of a series of layers having offset openings or a series of woven layers, which create a tortuous pathway for drug passage.

Preferably, the semi-permeable material is hydrophobic with openings of size selected to prevent substantial flow of aqueous drugs solutions from the region 28 until sufficient pressure is applied. Referring to Figs. 1a-1b, the water intrusion pressure of

the permeable hydrophobic material and that of the drug are selected such that the drug will not normally pass through the openings unless sufficient pressure is applied by inner the balloon 22. Selection of the proper intrusion pressure for the semi-permeable material 15 of the outer balloon 24 prevents passage of the drug 16 through the openings of the material 15 when the balloon is less than fully inflated.

As demonstrated in Fig. 1b, under conditions of sufficiently high intrusion pressure (e.g., with the balloon fully inflated), the drug 16 passes through the openings in a low-pressure, low-energy, non-injurious manner that applies the drug to the diseased tissue. The inner balloon 22 may be deflated, and the device may be refilled with drug, if necessary, and moved to various locations, where the inner balloon 22 is reinflated to deliver the drug 16 or a different concentration thereof, or another drug altogether to the various locations. This process may be repeated. A constant pressure pump may be used to maintain the balloon pressure above that needed to administer the drug through the openings during treatment. It will be understood that the dosage of the drug administered may also be carefully controlled by application of sufficient pressure to enable drug administration, then reducing the pressure below the threshold for passage through the openings, at which point, drug administration ceases. For example, the drug may be an aqueous solution of heparin and the semi-permeable material a patch of GORTEX®. Application of pressure above about 3 psi enables administration of the drug through the openings.

Various drugs can be administered, e.g., antithromhogenic drugs and antiproliferative drugs as listed herein in the summary of the invention. Preferably the drug is in aqueous solution. The

procedure can be performed in many body lumens, most preferably, the vascular system in which case dilatation of a stenosed blood vessel may be carried out before, after or simultaneously with drug application.

Other embodiments are within the claims.

Claims

1. A catheter for delivering drug to tissue at a desired location of the wall of a body lumen, comprising:

a catheter constructed for insertion in a body lumen having a catheter shaft and an expandable balloon portion mounted on said catheter shaft, said expandable balloon portion is expandable to a controlled pressure to fill the cross section of the body lumen and press - against the wall of said body lumen,

at least a portion of the exterior surface of the expandable balloon portion being defined by a porous membrane positioned over the surface of said balloon and creating therebetween a drug space, said porous membrane formed of a select material being constructed to release drug in said drug space through openings in said membrane to the outer surface of said membrane in a noninjurious low pressure manner, in response to pressure applied by inflation of said balloon to compress said drug space.

2. The catheter of claim 1 where said porous membrane has a series of tortuous pathways through its thickness between openings exposed to said drug space and openings exposed to said body lumen.

3. The catheter of claim 1 or 2 where said openings are of selected small size to prevent the flow of fluid prior to the application of pressure to said drug.

4. The catheter of claim 3 where said drug is an aqueous drug solution and said porous material is a hydrophobic material.

5. The catheter of claim 4 wherein said openings are in the range of about 2 to 20 μ.

6. The catheter of claim 1 wherein said material is selected from the group consisting of porous fluorocarbon plastic material and ultrahigh molecular weight microporous polyethylene.

7. The catheter of claim 1 wherein porous membrane comprises a plurality of layers of material, the orifice of which collectively define the tortuous pathways.

8. The catheter of claim 1 wherein said drug is an anti-thrombogenic drug selected from the group consisting of heparin, enoxaprin, aspirin, and hirudin.

9. The balloon catheter of claim 1 wherein said drug is an antiproliferative selected from the group consisting of monoclonal antibodies, capable of blocking smooth muscle cell proliferation, heparin and enoxaprin.

10. A method for delivering drug to the tissue at a desired location of the wall of a body lumen, comprising:

providing a catheter constructed for insertion in a body lumen having a catheter shaft having an expandable balloon portion mounted on said catheter shaft,

said expandable balloon portion being expandable to engage said tissue at a controlled pressure to fill the cross-section of the body lumen and press against the wall of said body lumen,

at least a portion of the exterior surface of the expandable portion being defined by a porous membrane

positioned over the surface of said balloon and creating therebetween a drug space,

said porous second material being constructed to release drug in said drug space through openings in said membrane to the outer surface of said membrane in a noninjurious, low pressure manner in response to pressure applied by inflation of said balloon to compress said drug space,

preparing said balloon portion by introducing an aqueous solution of said drug to said drug space,

introducing said catheter to said body lumen to position said expandable portion at the point of desired drug application, and

expanding said expandable balloon portion to enable delivery of said drug by compression of said drug space.

11. The method of claim 10 further comprising, deflating said balloon and repeating said preparing and expanding steps.

12. The method of claim 10 where said porous membrane has a series of tortuous pathways through its thickness between openings exposed to said drug space and openings exposed to said body lumen.

13. The method of claim 10 or 11 where said openings are of selected small size to prevent the flow of fluid prior to the application of pressure to said drug.

14. The method of claim 13 where said drug is an aqueous drug solution and said porous material is a hydrophobic material.

15. The method of claim 14 wherein said openings are in the range of about 2 to 20μ.

16. The method of claim 10 wherein said material is selected from the group consisting of porous fluorocarbon plastic material and ultrahigh molecular weight microporous polyethylene.

17. The method of claim 10 wherein said drug is an anti-thrombogenic drug selected form the group consisting of heparin, enoxaprin, aspirin, and hirudin.

18. The method of claim 10 wherein said drug is an antiproliferative selected from the group consisting of monoclonal antibodies capable of blocking smooth muscle cell proliferation, e.g., heparin and enoxaprin.

19. The method of claim 16 wherein said membrane comprises more than one layer of said material.

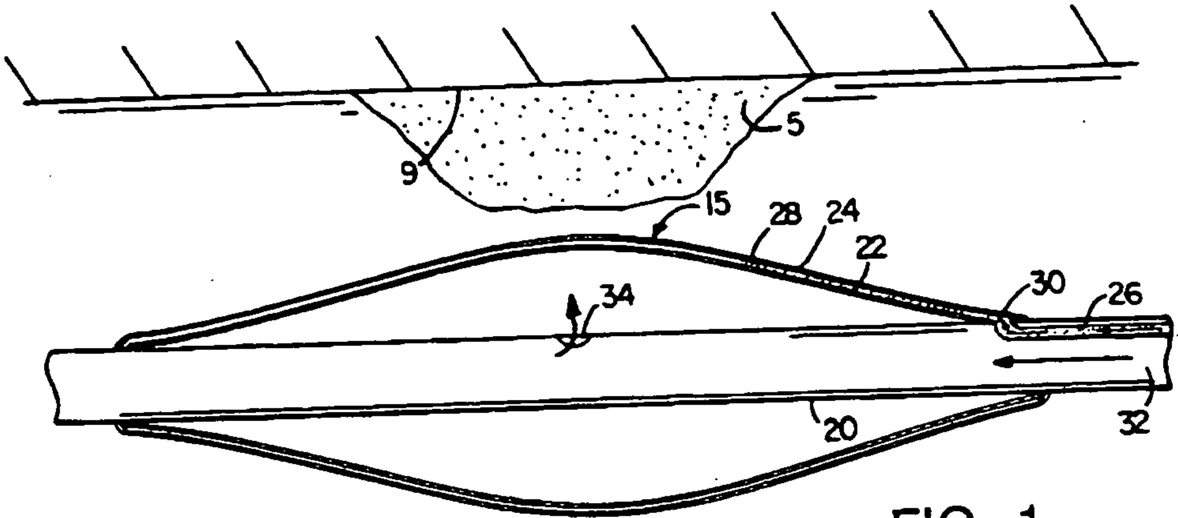

FIG. 1

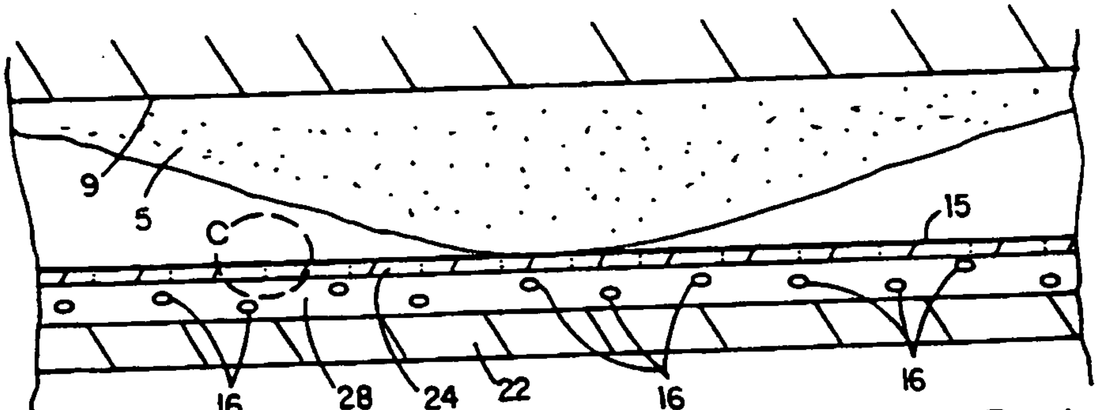

FIG. 1a

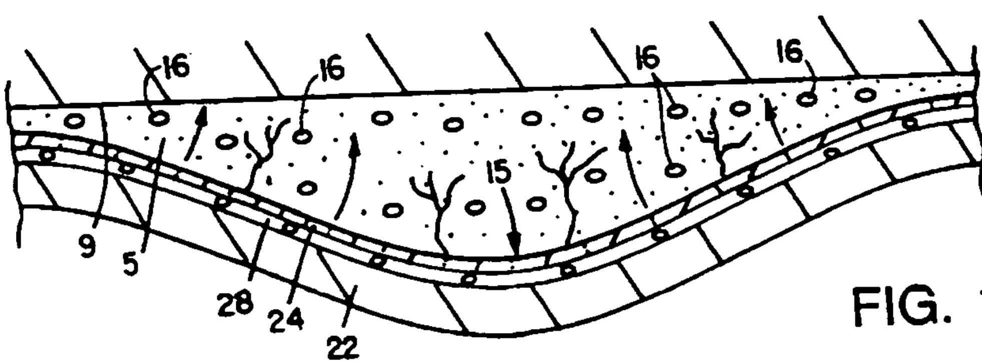

FIG. 1b

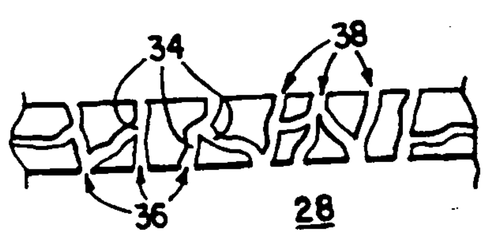

FIG. 1c